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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,985	12/19/2001	Carine Capiau	B45182	2966

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EXAMINER	
FORD, VANESSA L	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,985	CAPIAU ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-9,11,14 and 15* is/are pending in the application.

4a) Of the above claim(s) *12,14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-9 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 20, 2003 has been entered.

2. Applicant's amendment is acknowledged. Claim 1 has been amended. Claims 5, 10 and 13 have been cancelled.

3. The text of those sections of the Title 35, U.S. code not included in this action can be found in the prior Office Action.

Rejection Maintained

4. The rejection of claims under 35 U.S.C. 103(a) as unpatenable over Kuo et al in view of Masure et al maintained for claims 1-4, 6-9 and 11 the reasons set forth in paragraph 4, pages 2-9 of the previous Office Action.

The rejection was on the grounds that Kuo et al teach a composition comprising immunogenic polysaccharide-protein conjugates and pneumolysin protein of *Streptococcus pneumoniae* (see the Abstract). Kuo et al teach that capsular polysaccharides of various pneumococcal types (for example, types 6B, 14C, 18C and 20) are used in their inventions (column 5, lines 17-28 and column 6, Example 1). Kuo et al teach that the composition may be added to immunologically acceptable diluents or carriers in the conventional manner to prepare injectable liquid solutions or suspensions (column 5, lines 45-47). Kuo et al teach that the conjugates of the invention may be bound to aluminum hydroxide, aluminum phosphate (alum), QS-21, monophosphoryl lipid A and deacylated monophosphoryl lipid A (which induce strong TH1 responses) (column 5 lines 47-51). It is well known in the art to add protein carriers such as keyhole limpet haemocyanin (KLH), diphtheria toxoid, tetanus toxoid and protein derivative of Tuberculin (PPD) to antigens to enhance the immunogenicity of the antigen this is evidenced by *(U.S. Patent No. 6,419,932, U.S. Patent No. 4, 761, 283, U.S. Patent No. 6,224,880 and U.S. Patent No. 5,360,897).*

Kuo et al do not teach choline binding proteins.

Masure et al teach a vaccine comprising choline binding proteins (CBPs) (column 6, lines 65-67 and column 7, lines 1-8). Masure et al teach vaccines comprising CBP antigen or antigenic derivative or fragment thereof or a CBP nucleic acid vaccine that can be administered via any parenteral route including but not limited to intramuscular, intraperitoneal, intravenous and the like (column 24, lines 57-61). Masure et al suggest that criteria to consider in selecting a preferred CBP as a vaccine candidate includes testing CBP defective mutants for attenuation of virulence in animal models for bacteremia or colonization efficacy alone or in combination or coupled to a capsular polysaccharide (column 14, lines 41-46). Masure et al teach that the vaccines of the invention can be comprises an active material such as a diluent (i.e. carrier or vehicle) (column 29, lines 14-20). Masure et al teach that CBP or fragment thereof can be conjugated to an immunogenic carrier, e.g. bovine serum albumin (BSA) or keyhole limpet hemocyanin (KLH) (column 22, lines 5-8).

It would be *prima facie* obvious at the time the invention was made to add the CBP vaccines of Masure et al to the pneumococcal polysaccharide recombinant pneumolysin conjugate vaccines as taught by Kuo et al because Masure et al teach that one may administer the CBP vaccines in conjunction with one or more pharmaceutical compositions used for treating bacterial infection, including but no limited to antibiotics, soluble carbohydrate inhibitors of bacterial adhesion, other small molecule inhibitors of bacterial adhesion, inhibitors of bacterial metabolism, transport or transformation, stimulators of bacterial lysis or antibacterial antibodies or vaccines directed at other bacterial antigens (column 30, lines 34-42). It would be expected barring evidence to the contrary, that the addition of the CBP vaccines of Masure et al to the pneumococcal polysaccharide recombinant pneumolysin conjugate vaccines as taught by Kuo et al would be effective in treating *Streptococcus pneumoniae* infections.

Applicant urges that Kuo et al teach that conjugate vaccines of this invention are highly immunogenic in warm-blooded animals" and "the vaccines elicit antibodies to both the polysaccharide and the protein, recombinant pneumolysin". Applicant urges that the vaccine of Kuo et al possess all of the desired characteristics that one would require for a vaccine. Therefore, there is no motivation to add yet another component to a *Streptococcus pneumoniae* polysaccharide-conjugate composition. Applicant urges that the skilled artisan is acutely aware that when administering an immunogenic composition to elicit a protective immune response the fewer components that are combined to confer protection against infection is better. Applicant urges that there risk of immunological interference when more components are added to a vaccine. Applicant urges that the claimed invention is drawn to at least one *Streptococcus pneumoniae* polysaccharide-protein conjugate, at least one unconjugated *Streptococcus* protein antigen and an adjuvant which is a preferential inducer of TH1 response.

Applicant's arguments filed November 20, 2003 have been fully considered but they are not persuasive. There is no limitation or requirement in the claims that the composition comprises "at least one unconjugated *Streptococcus pneumoniae* protein antigen". The Examiner disagrees with Applicant's assertion that "the skilled artisan is acutely aware that when administering an immunogenic composition to elicit a protective immune response the fewer components that are combined to confer protection against infection is better and there is risk of immunological interference when more components are added to a vaccine" because Masure et al teach that one

may administer the CBP vaccines in conjunction with other vaccines because multi-component vaccines broaden and increase potential effectiveness of the vaccine (column 6, lines 65-67 and column 7, lines 1-8). One of skill in the art would be motivated to use the *Streptococcus pneumoniae* polysaccharide-protein conjugate and an adjuvant which is a preferential inducer of a TH1 response of Kuo et al in combination with the *Streptococcus pneumoniae* protein antigen (choline binding proteins) of Masure et al because both have been shown to be protective against *Streptococcus pneumoniae* infections. It should be noted that Masure et al teach that the choline binding proteins or fragments thereof mediated adhesion. One skill in the art would be motivated to add choline binding proteins or fragments thereof to other vaccine components to prevent bacteria from adhering to the cell surface, thereby preventing infection. If a bacterium cannot adhere to the cell surface then infection is minimized. The vaccine composition as taught by Kuo et al are used to target infections caused by *Streptococcus pneumoniae*. Therefore, a vaccine composition comprising the choline binding proteins or fragments thereof as taught by Masure et al and the polysaccharide-protein conjugates and adjuvants as taught by Kuo et al can be use as multi-component, multi-purpose vaccines for protection against pneumococcal infection.

There is nothing on the record to show that the combination of teachings would not suggest the claimed invention.

5. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is 571.272.0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at 571.272.0864.

Vanessa L. Ford
Biotechnology Examiner
February 25, 2004

L. F. Smith
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